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10/574,438	06/25/2007	Raymond Nadeson	210174.401USPC	9722

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EXAMINER	
JAGOE, DONNA A	

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1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/574,438	NADESON ET AL.	
	Examiner	Art Unit	
	Donna Jagoe	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *43-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *43-48* is/are rejected.

7)☒ Claim(s) *43* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 43-48 are presented for examination.

Claim Objections

Claim 43 is objected to because of the following informalities: the word "papveretum" is misspelled. The correct spelling is "papaveretum". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 43-48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In particular, claim 43 is drawn to flupirtine or a pharmaceutically acceptable salt thereof in combination with pharmaceutically acceptable derivates, homologs or analogs of the opioids detailed in the claim. The specification discloses chemicals, such as fentanyl, oxycodone, codeine, dihydrocodeine, dihydrocodeinone enol acetate, morphine, desomorphine, apomorphine, diamorphine, pethidine, methadone, dextropropoxyphene, pentazocine,

dextromoramide, oxymorphone, hydromorphone, dihydromorphine, noscapine, papverine, papveretum, alfentanil and buprenorphine which meet the written description and enablement provisions of 35 USC 112, first paragraph. However, claim 43 is directed to encompass derivates, analogs or homologs, which only correspond in some undefined way to specifically instantly disclosed chemicals. None of these derivates, analogs or homologs meet the written description provision of 35 USC § 112, first paragraph, due to lacking chemical structural information for what they are and chemical structures are highly variant and encompass a myriad of possibilities. The specification provides insufficient written description to support the genus encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of the above specifically disclosed chemical structures, the skilled artisan cannot envision the detailed chemical structure of the encompassed derivatives, analogs, etc., regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The chemical structure itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence. Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description

must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.

Therefore, only the above chemically structurally defined chemicals, but not the full breadth of the claim(s) meet the written description provision of 35 USC § 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC § 112 is severable from its enablement provision. (See page 1115.)

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 44-47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 44, 46 and 47 recites the limitation "the flupirtine" in each of the claims. There is insufficient antecedent basis for this limitation in the claim because the amendment dated June 25, 2007 removed the word "flupirtine" from instant claim 43.

Claims 45 is rejected as being indefinite because it depends from rejected claim 44.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 43-45 and 48 are rejected under 35 U.S.C. 102(e) as being anticipated by Klose et al. U.S. Patent No. 6,916,486 B2.

Klose et al. teach an analgesic composition (see abstract) for treatment of neuropathic pain (column 6, lines 55-59) comprising flupirtine (column 3, line 28) and other opioid analgesics such as buprenorphine, dextromoramide, dextropropoxyphen, diamorphine, fentanyl, alfentanyl, hydrocodone, hydromorphone, methadone, morphine, oxycodone, papaveretum, pentazocine, pethidine, codeine and dihydrocodeine. (column 3, line 28, and claims 5, 6, 11 and 12) for use in treatment of an animal, including a human (column 1, lines 19-20). Claims 11 and 12 of the patent describes the method of

administering **at least one** systemic acting analgesic to an animal wherein the analgesic is selected from the agents listed above.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 47 is rejected under 35 U.S.C. 103(a) as being unpatentable over Klose et al. U.S. Patent No. 6,916,486 B2 and Devulder at al. (U).

Klose et al. teach an analgesic composition (see abstract) for treatment of neuropathic pain (column 6, lines 55-59) comprising flupirtine and other opioid analgesics such as buprenorphine, dextromoramide, dextropropoxyphen, diamorphine, fentanyl, alfentanyl, hydrocodone, hydromorphone, methadone, morphine, oxycodone, papaveretum, pentazocine, pethidine, codeine and dihydrocodeine. (column 3, line 28, and claims 5, 6, 11 and 12) for use in treatment of an animal, including a human (column 1, lines 19-20). Claims 11 and 12 of the patent describes the method of administering **at least one** systemic acting analgesic to an animal wherein the analgesic is selected from the agents listed above.

Klose et al. does not teach the dose instantly recited in claim 47.

Devulder et al. teach the dose of flupirtine for treatment of neuropathic (central) pain is 300-600 mg/day. The instant claim is drawn to 0.5mg/kg to about 20 mg/kg of body weight. Translating the dose of Devulder et al. to mg/kg based on an average 80 kg human the dosage would be 3.75 mg/kg[1] to 7.5 mg/kg[2]. This dosage amount is encompassed by the claimed amount of 0.5 mg/kg to about 20 mg/kg. A prior art reference that discloses a range encompassing a somewhat narrower claimed range is sufficient to establish a prima facie case of obviousness." *In re Peterson*, 315 F.3d 1325, 1330, 65 USPQ2d 1379, 1382-83 (Fed. Cir. 2003). See also *In re Harris*, 409 F.3d 1339, 74 USPQ2d 1951 (Fed. Cir. 2005).

[1] 300 mg / 80 kg = 3.75 mg/kg

It would have been made obvious to one of ordinary skill in art at the time it was made to employ 0.5 mg/kg to about 20 mg/kg of flupirtine in the composition combined with another opioid agent to treat neuropathic pain motivated by the teaching of Klose et al. who teaches the combination for treatment of neuropathic pain and the teaching of Devulder et al. who teaches that the dosage of flupirtine for central (neuropathic) pain is 300 to 600 mg/day (approximately 3.75 mg/kg to about 7.5 mg/kg).

Claim 46 is rejected under 35 U.S.C. 103(a) as being unpatentable over Klose et al. U.S. Patent No. 6,916,486 B2 and Perovic et al. (V).

Klose et al. teach an analgesic composition (see abstract) for treatment of neuropathic pain (column 6, lines 55-59) comprising flupirtine and other opioid analgesics such as buprenorphine, dextromoramide, dextropropoxyphen, diamorphine, fentanyl, alfentanyl, hydrocodone, hydromorphone, methadone, morphine, oxycodone, papaveretum, pentazocine, pethidine, codeine and dihydrocodeine. (column 3, line 28, and claims 5, 6, 11 and 12) for use in treatment of an animal, including a human (column 1, lines 19-20). Claims 11 and 12 of the patent describes the method of administering **at least one** systemic acting analgesic to an animal wherein the analgesic is selected from the agents listed above.

Klose et al. does not disclose absence of overt sedation of opioids in the presence of flupirtine.

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[2] 600 mg / 80 kg = 7.5 mg/kg

Perovic et al. teach that flupirtine is a clinically safe compound with drowsiness reported in only 10% of cases (page 373, column 2). Since the dosage of the opioid is not disclosed, then the claim encompasses an almost negligible amount of opioid and as such overt sedation would not occur since it is dose related.

It would have been made obvious to one of ordinary skill in art at the time it was made to employ a non sedating combination of flupirtine and an opioid motivated by the teaching of Perovic et al. that flupirtine caused drowsiness in only 10 % of cases combined with the well known fact that sedation of opioid analgesics is dose related and since the claims do not disclose the dosage, they encompass a negligible amount of opioid.

Thus the claims fail to patentably distinguish over the state of the art as represented by the cited references.

Accordingly, for the above reasons, the claims are deemed properly rejected and none are allowed.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna Jagoe whose telephone number is (571) 272-0576. The examiner can normally be reached on Monday through Friday from 8:00 A.M. - 4:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Donna Jagoe /D. J./
Examiner
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September 12, 2008

/Ardin Marschel/
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